

61. (New) A composition having a synergistic neurotrophic activity, consisting of two cytokines, wherein the two cytokines are GDNF and TGF- $\beta$ , or functionally active derivatives or parts thereof, and further comprising a pharmaceutically acceptable carrier, diluent or any combination thereof.
62. (New) A composition having a synergistic neurotrophic activity consisting essentially of two cytokines, wherein the two cytokines are GDNF and TGF- $\beta$ , or functionally active derivatives thereof.

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#### REMARKS

##### Claim Amendments

Claim 1 has been amended to further define Applicants' invention. Support for this amendment, which does not broaden the scope of Applicants' claimed invention, can be found throughout the Specification, for example at page 2, line 25 through page 3, line 15.

Claims 57 and 58 have been amended to make clear that GDNF and TGF- $\beta$  are two cytokines. Support for these amendments can be found throughout the Specification, for example at page 2, line 25 through page 3, line 3, and page 3, lines 6-11.

New Claims 60-62 have been added. Support for these claims can be found throughout the Specification, for example at page 11, line 22 through page 13, line 8, and Figures 6A-D.

No new matter has been added.

##### Rejection of Claims 1, 2, 5, 16 and 57-59 Under 35 U.S.C. §102(b)

Claims 1, 2, 5, 16 and 57-59 are rejected by the Examiner under 35 U.S.C. §102(b) as being anticipated by Goulin *et al.* (J. Neurosci. Res. February 15, 1996).

In light of Applicants' cancellation of Claims 1, 2, 5, 16 and 59, the rejection of these claims is moot. With respect to Claims 57 and 58, Applicants respectfully disagree. Goulin *et al.* discloses the following compositions:

- (i) NGF + FGF-2 (for example, at p. 459)
- (ii) CNTF + FGF-2 (for example, at p. 459)

- (iii) TGF $\beta$ 3 + FGF-2 (for example, at p. 459, 460)
- (iv) GDNF +FGF-2 (for example, at p. 460)
- (v) TGF $\beta$ 3 +GDNF + FGF-2 (for example, at p. 461)

Claims 57 and 58, as amended, recite a “composition having synergistic neurotrophic activity consisting of two cytokines, wherein the two cytokines are GDNF and TGF- $\beta$ ....” Applicants amendment to recite “two cytokines” is to further make clear that GDNF and TGF- $\beta$  are cytokines, although this was already well known to one of ordinary skill in the art at the time of filing of the application. Goulin *et al.* do not disclose a composition consisting of GDNF and TGF- $\beta$ , thus Goulin *et al.* does not anticipate Claims 57 and 58, as amended.

Furthermore, the Examiner has stated that the serum-free culture medium of Goulin *et al.* is a pharmaceutically-acceptable carrier, diluent, or any combination thereof (Office Action, page 3). However, Applicants respectfully disagree because one of ordinary skill in the art would not consider complete basal medium containing, *inter alia*, insulin, sodium selenite, progesterone, putrescine, penicillin and streptomycin (page 455, column 1-2, bridging paragraph) a pharmaceutically-acceptable carrier or diluent. The combination of these hormones and antibiotics together with putrescine (defined in Stedman’s Medical Dictionary, 26<sup>th</sup> Edition, as “a poisonous polyamine”, attached as Exhibit A) and sodium selenite (which, in high quantities is known to be toxic, see the Material Safety Data Sheet obtained from Sigma Chemical Co., attached as Exhibit B), would not be considered a pharmaceutically-acceptable carrier or diluent by one of ordinary skill in the art.

Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claim 59 Under 35 U.S.C. §112, Second Paragraph

Claim 59 is rejected by the Examiner under 35 U.S.C. §112, Second Paragraph “as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” In view of Applicants’ cancellation of Claim 59, the rejection is moot.

Provisional Double-Patenting Objection

The Examiner advised the Applicants that should Claim 57 be found allowable, Claim 59 will be "objected to under 37 C.F.R. 1.75 as being a substantial duplicate thereof." As noted above, Applicants have cancelled Claim 59, thus the rejection is moot.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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MARKED UP VERSION OF AMENDMENTSClaim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

- 1 (Four Times Amended) A composition having synergistic neurotrophic activity, comprising at least two cytokines, or functionally active derivatives or parts thereof of said cytokines, wherein at least one of said cytokines is BMP, GDF, TGF- $\beta$  or GDNF, and wherein if a first cytokine is TGF- $\beta$ , then a second cytokine is not NT-3, NT-4 or FGF, and wherein if a first cytokine is GDNF, then a second cytokine is not FGF.
57. (Twice Amended) A composition having a synergistic neurotrophic activity, comprising two cytokines, wherein the two cytokines are GDNF and TGF- $\beta$ , or functionally active derivatives or parts thereof.
58. (Twice Amended) A composition having a synergistic neurotrophic activity, comprising two cytokines, wherein the two cytokines are GDNF and TGF- $\beta$ , or functionally active derivatives or parts thereof, and further comprising a pharmaceutically acceptable carrier, diluent or any combination thereof.